OMB INFORMATION COLLECTION
SUPPORTING STATEMENT

Regulations for In Vivo Radiopharmaceuticals Used for Diagnosis and Monitoring
0910-0409

JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting OMB approval of the information collection requirements contained in 21 CFR 315.4 through 315.6 and in 21 CFR 601.33 through 601.35 (Attachment A). The requirements for which approval is requested are:

21 CFR 315.4, 315.5, and 315.6	Reporting	Manufacturers of diagnostic radiopharmaceuticals shall submit information that demonstrates the safety and effectiveness of a new diagnostic radiopharmaceutical or of a new indication for use of an approved diagnostic radiopharmaceutical.
21 CFR 601.33, 601.34, 601.35	Reporting	Manufacturers of diagnostic radiopharmaceuticals shall submit information that demonstrates the safety and effectiveness of a new diagnostic radiopharmaceutical or of a new indication for use of an approved diagnostic radiopharmaceutical.

In response to the requirements of section 122 of the Food and Drug Administration Modernization Act of 1997 (FDAMA)(P.L. 105-115)(Attachment B), FDA is amending the drug and biologics regulations by adding provisions that would clarify FDA's evaluation and approval of in vivo radiopharmaceuticals used in the diagnosis or monitoring of diseases. The regulations will describe the kinds of indications of diagnostic radiopharmaceuticals and some of the criteria that the agency would use to evaluate the safety and effectiveness of a diagnostic radiopharmaceutical under the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) (Attachment C) and section 351 of the Public Health Service Act (42 U.S.C. 262) (Attachment D).

In the Federal Register of May 22, 1998 (63 FR 28301)(Attachment E), FDA published the proposed rule to implement section 122 of FDAMA. The information collection package for the proposed rule was submitted for approval to OMB on 5/21/98. The package was not approved by OMB citing concerns regarding the utility and burden of the information collected to demonstrate the safety and effectiveness of a new diagnostic radiopharmaceutical or of a new indication for use of an approved diagnostic radiopharmaceutical. OMB stated that the burden and utility should be assessed in light of public comments received in response to the proposed rule. FDA received one comment on the information collection provisions of the proposed rule. Comments in response to the proposed rule are discussed in Section 8 of this supporting statement.

2. Purpose and Use of the Information

Information about the safety or effectiveness of a diagnostic radiopharmaceutical would enable the

agency to properly evaluate the safety and effectiveness profiles of a new diagnostic radiopharmaceutical or a new indication for use of an approved diagnostic radiopharmaceutical, as required under section 505 of the Federal Food, Drug, and Cosmetic Act and section 351 of the Public Health Service Act.

3. Use of Information Technology and Burden Reduction

One of FDA's continuing objectives is to improve the speed and quality of its review and approval programs. In order to reach a decision to approve an application the agency must evaluate all information and data provided by applicants that support the safety, purity, potency, and efficacy of the proposed product. To make the review process more efficient for industry and FDA, CBER and CDER are utilizing electronic information systems technology. CBER accepts "Computer Assisted Product License Applications" (CAPLA) and CDER encourages sponsors to use "Computer Assisted New Drug Applications" (CANDA). FDA believes the increased use of computer assisted application will enhance the timeliness, effectiveness, and efficiency of the review process and reduce burdensome, nonessential hard-copy handling and storage. FDA is not aware of any other improved technology to reduce the burden.

4. Efforts to Identify Duplication and Use of Similar Information

FDA is the only agency that requires the filing of an application for the marketing of diagnostic radiopharmaceuticals for human use. No other component of the agency or other government agencies require similar information or data to be filed. The information to be submitted under the regulations is not available from any other source.

. Impact on Small Businesses or Other Entities

FDA believes that its duty requires the equal application of the regulations to all enterprises. While FDA does not believe it can apply different standards with respect to statutory requirements, FDA does provide special help to small businesses. The Center for Biologics Evaluation and Research, Office of Communications, Training, and Manufacturers Assistance provides assistance to small businesses subject to FDA's regulatory requirements. FDA determined that of the approximately 8 entities estimated to be affected by the final rule, only 2 would be considered "small" under criteria established by the Small Business Administration.

6. Consequences of Collecting the Information Less Frequently

Manufacturers submit applications for approval of a diagnostic radiopharmaceutical to obtain permission to market the product in interstate commerce. Less frequent collection of information or other methods of reducing the frequency of information would not provide the information needed by FDA to properly evaluate the safety and effectiveness of a diagnostic radiopharmaceutical or a new indication for use of an approved diagnostic radiopharmaceutical. There are no technical or legal obstacles to reducing the burden.

7. Special Circumstances Relating to the Guideline of 5 CFR 1320.5

An applicant may be required to submit to FDA proprietary trade secrets or other confidential information when submitting a license application or supplement. FDA has instituted security measures to protect confidential information received from manufacturers and will, to the extent permitted by law, protect this information.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In the Federal Register of May 22, 1998, FDA published the proposed rule and provided a 30-day notice requesting comments from the public on the information collection provisions. FDA received one comment on these provisions. The comment stated that use of the figure of 7 approved diagnostic radiopharmaceuticals in fiscal year (FY) 1997 resulted in a very low estimate of the expected number of future annual applications. The comments suggested that 50 applications would be more appropriate.

Based on past experience, FDA believes that its estimate of the number of applications for approval of in vivo diagnostic radiopharmaceuticals is reasonable. In FY 1992 to 1997, FDA approved 13 in vivo diagnostic radiopharmaceuticals. In FY 98, only one such product was approved. FDA does not expect an increase in applications for approval of diagnostic radiopharmaceuticals in the near future. Although sponsors may submit a higher number of IND's for diagnostic radiopharmaceuticals each year, the annual number of marketing applications (NDA's, ANDA's, BLA's) approved is small. Therefore, no change was made to the estimate.

As stated previously, OMB maintained that the burden and utility of this information collection should be assessed in light of public comments on the proposed rule. As discussed above, only one comment was received on the information collection provisions of the proposed rule. None of the manufacturers of diagnostic radiopharmaceuticals who submitted comments on the proposed rule questioned the need for submission of information to demonstrate the safety and effectiveness of a product to obtain marketing approval. Rather, their comments primarily sought clarification or proposed minor modification of the proposed regulations. These comments were addressed in the preamble of the final rule.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift was provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

The confidentiality of information received by FDA under the final rule would be consistent with the Freedom of Information Act and the agency's regulations under 21 CFR Part 20. Manufacturers seeking to have a diagnostic radiopharmaceutical or a new indication for use for an approved diagnostic radiopharmaceutical might be required to reveal proprietary information or trade secrets to gain FDA approval of the product or new indication. However, such information is deleted from the application before it is released under the Freedom of Information Act and FDA regulations.

11. Justification for Sensitive Questions

Questions of a sensitive nature are not applicable to this information collection.

12. Estimate of Hour Burden Including Annualized Hourly Costs

The estimated current annual burden for this information collection is 16,000 hours.

Estimated Annual Reporting Burden

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
315.4, 315.5, and 315.6	3	1	3	2,000	6,000
601.33, 601.34, and 601.35	5	1	5	2,000	10,000
TOTAL	8		8		16,000

To estimate the potential number of respondents that would submit applications or supplements for diagnostic radiopharmaceuticals, FDA used the number of approvals granted in FY 1997 to approximate the number of future annual applications. In FY 1997, FDA approved 7 diagnostic radiopharmaceuticals and received 1 new indication supplement; of these, 3 respondents received approval through CDER and 5 received approval through CBER. The annual frequency per response was estimated be one response per application or supplement. The hours per response refers to the estimated number of hours that an applicant would spend preparing the information required by the final regulations. Based on FDA's experience, the agency estimates the time needed to prepare a complete application for a diagnostic radiopharmaceutical approximately 10,000 hours, roughly one-fifth of which, or 2,000 hours, is estimated to be spent preparing the portions of the application that would be affected by these final regulations. The final rule would not impose any additional reporting burden for safety and effectiveness information on diagnostic radiopharmaceuticals beyond the estimated current burden of 2,000 hours because safety and effectiveness information is already required by § 314.50 under OMB control number 0910-0001 and § 601.2 under OMB control number 0910-0124. In fact, clarification in the final rule of FDA's standards for evaluation of diagnostic radiopharmaceuticals is expected to streamline overall information collection burdens, particularly for diagnostic radiopharmaceuticals that may have well-established low-risk safety profiles, by enabling manufacturers to tailor information submissions and avoid unnecessary clinical studies. The table above indicates estimates of the annual reporting burdens for the preparation of the safety and effectiveness sections of an application that are imposed by existing regulations, §§ 314.50 and 601.2. The burden totals do not include an increase in burden because no increase is anticipated. This estimate does not include the actual time needed to conduct studies and trials or other research from which the reported information is obtained.

Cost to Respondents

The estimated annual cost to respondents is $498,400.00.

Activity	No. of Hours	Cost per hour	Total Cost
Reporting	16,000	$31.15	$498,400.00

FDA estimates that it should require an average of 2,000 hours of staff time per applicant to organize and submit the required safety and effectiveness information portions of a new application or supplement to an approved application. The estimate is based on a regulatory affairs specialist, at a pay rate of $31.15/hour, who is responsible for preparing the safety and effectiveness portions of an application or supplement. The salary estimates include benefits but no overhead costs.

13. Estimate of Other Total Annual Cost Burden to Respondents of Recordkeepers

There are no capital and start-up, and operation, maintenance and purchase costs associated with the information collection.

14. Annualized Cost to the Federal Government

An estimate of the total cost to the Federal Government associated with the review of New Drug Applications, Product License Applications, Establishment License Applications, and supplemental applications is provided in the table below. The estimate is based on full-time equivalents (FTEs) associated with the review of applications and supplements to applications and the average annual salaries for CBER and CDER reviewers. The cost estimate for the review of information submitted under existing regulations is $34,109, 598.00, which is not expected to increase under the final regulations.

The amount of time and expense incurred by the government is due to the review of all material submitted with an application. This information is essential to determine the safety and effectiveness of products as required by FDA's mission to protect the public health. This information may include clinical data, safety updates, samples submitted for evaluation by the agency, case report tabulations, case report forms, and patient information.

Applications[1]	Number of FTEs	Average Annual Reviewer Salary	Total Cost
NDA[2]	327	$70,834.00	$23,162,718.00
ELA[3] and PLA[4]	168	$65,160.00	$10,946,880.00
Total Cost to Government			$34,109,598.00

1 Includes original applications and supplements to approved applications.
2 New Drug Application
3 Establishment License Application
4 Product License Application

15. Explanation of Program Changes or Adjustments

Changes in burdens is not applicable as this is the first submission for the final rule.

16. Plans for Tabulation and Publication and Program Time Schedule

There are no tabulated results to publish for this information collection.

17. Reason(s) Display of Expiration Date is Inappropriate

FDA is not seeking approval to exempt the display of the expiration date of the OMB approval.

18. Exceptions to Certification for Paperwork Reduction Act Submission

There are no exceptions to Item 19 of OMB Form 83-I.